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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,802	06/19/2003	Jennie P. Mather	415072002500	9712

25226 7590 06/18/2008

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
06/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,802	MATHER ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *3-11 and 16-24* is/are withdrawn from consideration.

5)☒ Claim(s) *15 and 25* is/are allowed.

6)☒ Claim(s) *1,2,12-14 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/16/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant adds new claims 2-26.

Accordingly, Group A, claims 1-2, 12-15, 25-26, species lung cancer are examined in the instant application.

The embodiment of claims 1-2, 12-14, 26 as being drawn to species cancers other than lung cancer, as recited in claim 2, have been withdrawn from consideration as being drawn to non-elected species.

Withdrawn Rejection

The following rejections have been withdrawn: 1) Deposit requirement, 2) Sequence rule in view of the amendment of the specification on 08/04/06, 3) 112, second paragraph, in view of the amendment and arguments, 4) 112, first paragraph concerning the enablement of the antibody produced by the hybridoma cell line PTA-4244 as claimed in claim 15 to detect lung cancer, in view of the arguments, and 5) 102, in view of the amendment. The 102 rejection could be reinstated if the amendment of claim 1 were cancelled.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 12-14, 26 are rejected under 112, first paragraph for lack of a clear written description of the "conformational epitope" of B7H3L.

The response asserts that the specification discloses the three epitopes A-C to which the claimed antibodies bind (p.61-62, para 175).

The response has been considered but is not found to be persuasive for the following reasons:

Although the specification discloses that the antibody epitopes can be linear or conformational (para 0087 on page 30), the specification does not describe which epitopes on B7H3L are conformational epitopes. The specification only discloses that epitopes A-C are on amino acids 1-349 of the full length B7H3 comprising amino acids 1-534 (Table 3 on page 67). However, one cannot predict whether these epitopes are conformational, because an epitope of an antibody could be linear or conformational. Antibodies bind to structural shapes that may be linear stretches of amino acids, or conformational determinants formed by the folding of peptides, carbohydrate moieties, phosphate or lipid residues or a combination thereof.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1-2, 12-14, 26 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for an antibody that binds to a conformational epitope of B7H3L, and is able to deliver a therapeutic agent to a cancer cell expressing B7H3L.

1) The ability of the claimed antibody to deliver a therapeutic agent to a cancer cell

The response asserts that the specification teaches how to use the antibodies of the claimed invention for therapeutic purposes (see Section VIII, pages 39 to 48). The responses

asserts that Example 14 is a working example of in vitro cancer cell growth reduction using antibodies of the claimed invention with a toxin conjugate.

The response has been considered but is not found to be persuasive for the following reasons:

Claims 1-2, 12-14, 26 encompass an antibody that could be used for in vivo treating cancer that expresses B7H3L.

One cannot extrapolate from an example of in vitro cancer cell killing to in vivo treating cancer. Zips et al, 2005, In vivo, 19: 1-8, who teach that prediction of drug effects in cancer patients **based solely** on **in vitro data is not reliable** and further evaluation in animal tumor systems is essential (p.3, second column, last paragraph). Zips et al teach that despite their importance for drug testing, in vitro methods are beset by pitfalls and inherent limitation (p.3). Zips et al further teach that cells in culture represent an artificial and simplified system, and that unlike in vitro situation, a tumor is a 3-dimension complex consisting of interacting malignant and non-malignant cells (p.3, second column, last paragraph). Zips et al further teach that vascularisation, perfusion and thereby, drug access to the tumor cells are not evenly distributed and this fact consists an important source of of heterogeneity in tumor response to drugs that does not exist in vitro (p.3, second column, last paragraph). Lee et al, 1999, J Immunol, 163: 6292-6300, teach that although in vitro sensitization assays increase melanoma specific CTL reactivity with melanoma peptide, such response is not associated with tumor regression (abstract). Kirkin et al, 1998, APMIS, 106 : 665-679, of record, teach that although several peptides of melanoma associated antigens have been identified as being able to induce CTLs, which could lyse cancer cells in vitro, and in particular peptides from MAGE-A1 and MAGE-A3

have been tested for their ability to induce anti-melanoma immune response in vivo, so far only **one** of the peptides, peptide EVDPIGHLY of MAGE-A3, has limited anti-tumor activity (p.666, second column, second paragraph, last 6 lines). Dermer, 1994 (Bio/Technology, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary -type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions.

Further, cancer immunotherapy is unpredictable, in view of the teaching of White et al, Kirkin et al, Boon, Smith et al, and Bodey et al, all of record.

2) Conformational epitope of B7H3L.

The response asserts that the specification discloses the three epitopes A-C to which the claimed antibodies bind (p.61-62, para 175).

The response has been considered but is not found to be persuasive for the following reasons:

One cannot predict which of the epitopes on B7H3L of the claimed antibodies are **conformational epitopes**. Although the specification discloses that the antibody epitopes can be linear or conformational (para 0087 on page 30), the specification does not describe which epitopes on B7H3L are conformational epitopes. The specification only discloses that epitopes A-C are on amino acids 1-349 of the full length B7H3 comprising amino acids 1-534 (Table 3 on page 67). However, one cannot predict whether these epitopes are conformational, because an epitope of an antibody could be linear or conformational. Antibodies bind to structural shapes that may be linear stretches of amino acids, or conformational determinants formed by the folding of peptides, carbohydrate moieties, phosphate or lipid residues or a combination thereof.

Conclusion

Claims 15, 25 are free of prior art and are allowable.

Claims 1-2, 12-14, 26 are rejected for reasons set forth above.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
June 10, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643